

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of

SCHWEIGHOFFER et al.

Atty. Ref.: 3665-167; Confirmation No. 5165

Appl. No. 10/560,774

TC/A.U. 1617

Filed: December 14, 2005

Examiner: Javanmard

For: USE OF PYRAZOLOPYRIDINES FOR THE TREATMENT OF COGNITIVE  
DEFICITS

\* \* \* \* \*

May 11, 2009

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**REQUEST FOR RETURN OF INITIALED COPY OF PTO 1449 FORM FILED  
JANUARY 23, 2009**

Return of an initialed copy of the PTO 1449 Forms filed January 23, 2009 is requested.

The Examiner states in the Office Action dated April 20, 2009 that the documents cited in the PTO 1449 Form were not available to the Examiner at the time of the mailing of the Office Action.

The applicants submit, with due respect to the Examiner, that the references noted below were contained in the PTO IFW as of January 23, 2009. Consideration of the following in this regard is required.

A copy of the following listed documents is not contained in the PTO IFW and were not filed January 23, 2009: Brighina et al, "Recent Advances in the Therapy of

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Amyotrophic Lateral Sclerosis: Focus on Excitotoxicity", FUNCTIONAL NEUROLOGY (16), Suppl. 4, 2001, pp. 189-292; and Rowland et al, "Amyotrophic Lateral Sclerosis", N. ENGL. J. MED., Vol, 344, No. 22, May 31, 2001, pp. 1688-1700. The undersigned has requested a copy of these documents and will file same once received by the undersigned.

The following is a screen shot of the PTO IFW on May 10, 2009:

[illegible]

The above screen shot of the IFW demonstrates that the following documents were contained in the IFW when the Office Action of April 20, 2009 was mailed:

1. 01-23-2009 NPL Documents PROSECUTION (11 pages)
2. 01-23-2009 NPL NPL Documents PROSECUTION (180 pages)
3. 01-23-2009 NPL NPL Documents PROSECUTION (6 pages)
4. 01-23-2009 NPL NPL Documents PROSECUTION (10 pages)
5. 01-23-2009 NPL NPL Documents PROSECUTION (26 pages)
6. 01-23-2009 NPL NPL Documents PROSECUTION (7 pages)
7. 01-23-2009 NPL NPL Documents PROSECUTION (2 pages)
8. 01-23-2009 NPL NPL Documents PROSECUTION (13 pages)
9. 01-23-2009 NPL NPL Documents PROSECUTION (6 pages)
10. 01-23-2009 NPL NPL Documents PROSECUTION (4 pages)
11. 01-23-2009 NPL NPL Documents PROSECUTION (4 pages)
12. 01-23-2009 NPL NPL Documents PROSECUTION (2 pages)
13. 01-23-2009 NPL NPL Documents PROSECUTION (12 pages)
14. 01-23-2009 NPL NPL Documents PROSECUTION (7 pages)
15. 01-23-2009 FOR Foreign Reference PROSECUTION (48 pages)
16. 01-23-2009 FOR Foreign Reference PROSECUTION (46 pages)

Item 1. listed above contains the "Claims filed December 15, 2008 in Application No. 10/486,639" listed on the PTO 1449 Form filed January 23, 2009.

Item 2, listed above contains the following documents listed on the PTO 1449 Form filed January 23, 2009:

"Claims filed December 15, 2008 in Application No. 10/486,639";

Pitt et al. "Glutamate Excitotoxicity in a Model of Multiple Sclerosis". *Nature*.  
2000; 6(1):67-70;

Bever et al. The effects of 4-aminopyridine in multiple sclerosis patients: Results  
of a randomized, double-blind, placebocontrolled, crossover-trial. *Neurology*, 1994 Vol.  
44:1054-1059;

Bever et al. Treatment with oral 3,4 diaminopyridine improves leg strength in  
multiple sclerosis patients: Results of a randomized, double-blind, placebo-controlled,  
crossover-trial. *Neurology*, 1996 Vol. 47:1457-1462;

Rasdn et al. Cloning and characterization of a CAMP-specific phosphodiesterase  
(TbPDE2B) from *Trypanosoma brucei*. *PNAS*, 2002 Vol. 99:4714-4719;

Ward et al., "Pentoxifylline-A Review of its Pharmacodynamic and  
Pharmacokinetic Properties, and its Therapeutic Efficacy", *Drug Evaluation, Drugs* 34:  
50-97 (1987);

Leigh et al., "Excitotoxicity in ALS", *Nerol*. 1996 47 (Supp 4), S221-7;

Ludolph et al., "The role of excitotoxicity in ALS - what is the evidence?", *J. of*  
*Neurol*. 2000, 247 (Supp 1) 7-16;

Rothstein, "Excitotoxicity and Neurodegeneration in Amyotrophic Lateral  
Sclerosis", *Clin Neurosc* 95-96 3(6) 348-59;

Rothstein, "Excitotoxicity hypothesis", *Neurol* 1996 47 (Supp 4) S19-25;

Doble, "The pharmacology and mechanism of action of riluzole", *AMERICAN*  
*ACADEMY OF NEUROLOGY*, 1996, pp. S233-S241;

Bar, "Motor neuron disease in vitro: the use of cultured motor neurons to study amyotrophic lateral sclerosis", EUROPEAN JOURNAL OF PHARMACOLOGY, 405, 2000, pp. 285-295;

Sommer et al, "Therapeutic potential of phosphodiesterase type 4inhibition in chronic autoimmune demyelinating disease", JOURNAL OF NEUROIMMUNOLOGY, 79, 1997, pp. 54-61;

Beghi et al, "A randomized controlled trial of recombinant interferon beta-1a in ALS", AMERICAN ACADEMY OF NEUROLOGY, 2000, pp. 469-473;

Jahn et al, "Mechanism of block of nicotinic acetylcholine receptor channels by purified IgG from seropositive patients with myasthenia gravis, AMERICAN ACADEMY OF NEUROLOGY, 2000, p. 474;

Asahara et al, "Glutamate enhances phosphorylation of neurofilaments in cerebellar granule cell culture", JOURNAL OF THE NEUROLOGICAL SCIENCES, 171, 1999, 84-87 (first page attached);

Houslay, PROGRESS IN NUCLEIN ACID RESEARCH AND MOLECULAR BIOLOGY, Vol. 69, 1001, 249-315 (first page attached);

Snider et al, "Signaling the Pathway to Regeneration", NEURON 2002, 35, 13-6 (first page attached);

Santos et al, "Cyclic AMP increases the survival of ganglion cells in mixed retinal cell cultures in the absence of exogenous neurotrophic molecules, an effect that involves cholinergic activity", BRAZ J. MED BIOL RES, 2001m, 34, 1585-1593, pp. 1585-1593 (first page attached);

Feldman et al, "Breathing: Rhythmicity, Plasticity, Chemosensitivity", ANNU REV NEUROSCI 2003, 26, pp. 239-266 (first page attached);

Polman et al, "Clinical review: Drug treatment of multiple sclerosis", BMJ, Volume 321, 19-26 August 2000, pp. 490-494; and

Compston et al, "Multiple sclerosis", THE LANCET, Vol. 359, April 6, 2002, pp. 1221-31.

Item 3, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Branch, "A good antisense molecule is hard to find", TIBS, 23, February 1998, pp. 45-50.

Item 4, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Cherry et al, "Diazepam and rolipram differentially inhibit cyclic AMP-specific phosphodiesterases PDE4A1 and PDE4BE in the mouse", BIOCHEMICA ET BIOPHYSICA ACTA 1518, 2001 PP. 27-35.

Item 5, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Crooke, "Basic Principles of Antisense Therapeutics", Chapter 1, pp. 1-50.

Item 6, listed above contains the following document listed on the PTO 1449 Form filed January 23, 2009:

Dinter, "Phosphodiesterase Type 4 Inhibitors", BioDrugs, Feb. 2000, 13 (2), pp. 87-94.

Item 7, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Friedman et al, "A Pilot Study of Pentoxifylline in Multiple Schlerosis",

ARCHIVES OF NEUROLOGY, October 1996, Vol. 53, pp. 956-957.

Item 8, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Jen et al, "Suppression of Gene Expression by Targeted Disruption of  
Messenger RNA: Available Options and Current Strategies", STEM CELLS 2000,  
18:307-319.

Item 9, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Kempermann et al, "Functional significance of adult neurogenesis", Current  
Opinion in Neurobiology 2004, 14:186-191.

Item 10, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Mishra et al, "Calcium calmodulin and 3',5'-cyclic nucleotide phosphodiesterase  
activity in human muscular disorders", JOURNAL OF THE NEUROLOGICAL  
SCIENCES, 109, 1992, 215-218.

Item 11, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Myers et al, "Pentoxifylline is not a promising treatment for multiple sclerosis in  
progression phase", AMERICAN ACADEMY OF NEUROLOGY, 1998, pp. 1483-1486.

Item 12, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Pihl-Carey, "Isis to Restructure as Crohn's Disease Drug Falls in Phase III",

BIOWORLD TODAY, vol. 10, 239, December 1999, pp. 1-2.

Item 13, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

Price et al, "Mémoire: Amyotrophic lateral sclerosis and Alzheimer's disease. Lessons from model systems", REV NEUROL (PARIS), 1997, 153: 8-9, pp. 484-495.

Item 14, listed above contains the following document listed on the PTO 1449

Form filed January 23, 2009:

van Oosten, "A pilot study investigating the effects of orally administered pentoxifylline on selected immune variables in patients with multiple sclerosis", JOURNAL OF NEUROIMMUNOLOGY, 1996, 66, pp. 49-55.

Item 15, listed above contains WO 00/40714, which is n listed on the PTO 1449

Form filed January 23, 2009.

Item 16, listed above contains WO 01/44449, which is n listed on the PTO 1449

Form filed January 23, 2009.

A copy of the following listed documents is not contained in the PTO IFW and were not filed January 23, 2009: Brighina et al, "Recent Advances in the Therapy of Amyotrophic Lateral Sclerosis: Focus on Excitotoxicity", FUNCTIONAL NEUROLOGY (16), Suppl. 4, 2001, pp. 189-292; and Rowland et al, "Amyotrophic Lateral Sclerosis", N. ENGL. J. MED., Vol, 344, No. 22, May 31, 2001, pp. 1688-1700. The undersigned



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has requested a copy of these documents and will file same once received by the undersigned.

The following is a copy of the undersigned's receipts from the January 23, 2009 filing of the listed documents.

May 11, 2009

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JANUARY 23, 2009

Electronic Acknowledgement Receipt	
EFS ID:	4656546
Application Number:	10560774
International Application Number:	
Confirmation Number:	5165
Title of Invention:	Use of pyrazolopyridines for the treatment of cognitive deficit
First Named Inventor/Applicant Name:	Fabien Schweighoffer
Customer Number:	22117
Filer:	B.J. Sadoff/Pachack Phommachanh
Filer Authorized By:	B.J. Sadoff
Attorney Docket Number:	BUS-3665-167
Receipt Date:	23-JAN-2009
Filing Date:	14-DEC-2005
Time Stamp:	19:22:36
Application Type:	U.S. National Stage under 35 USC 371

**Payment information:**

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	5180
RAM confirmation Number	761
Deposit Account	
Authorized User	

**File Listing:**

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part (.zip)	Pages (if appl.)
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JANUARY 23, 2009

Return of an initialed copy of the PTO 1449 Forms filed January 23, 2009, as acknowledgement of consideration of the filed documents, pursuant to MPEP § 609, is requested.

The present Request is not being filed in response to the Office Action of April 20, 2009.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By:                     /B. J. Sadoff/                    

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